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LUD 5253.5 DIV-JEL/NDH (09885911)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Thierry BOON-FALLEUR et al.
Serial No.	:	08/819,669
Filed	:	March 17, 1997
For	:	TUMOR, REJECTION, ANTIGEN PRECURSORS, TUMOR REJECTION ANTIGENS AND USES THEREOF
Art Unit	:	1644
Examiner	:	P. Gamble

December 31 , 2002

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

RESPONSE TO
OFFICE ACTION
(37 CFR §1.111)

This is submitted in response to the office action dated October 1, 2002. Claims 183-191 are pending. Hence, the reference to claims 19-25 as set forth in the office action is obscure.

Applicants have considered each of the points raised by the examiner in the office action of October 1, 2002, and traverse each.

First, applicants turn to point 5 of the office action, which is obscure. The examiner appears to be taking the position that deposit is necessary to satisfy the enablement requirement and to practice the claimed invention. Why the examiner has taken this position is obscure. While the examiner states that

"It is apparent that the original clones to re-sequence the 1.7/1.8 cDNA molecules disclosed in the specification as filed is required to practice the claimed invention," the examiner has not explained the basis for his opinion. Further, applicants do not agree that deposit is necessary.

The declaration makes absolutely clear, at paragraph 8, that

> "Pierre Van der Bruggen was able to ascertain that there were still frozen samples of E. coli available which contained copies of the 1.7kb cDNA clone he had sequenced on July 4, 1991. He had a sample of these bacteria thawed, their viability confirmed, and had the 1.7kb cDNA inserts sequenced, on April 25, 2000."

Clearly, they were the same sequences. The specification refers to the sequence as 1.8 Kilobases, but as the declaration points out:

> "The 1.8 kilobase cDNA molecule referred to in the specification and the 1.7 kilobase cDNA molecule referred to in our declaration of July 9, 1998, are the same molecule."

See paragraph 3.

The specification describes, in great detail, how this 1.7/1.8 kb cDNA molecule was obtained. A very thorough and complete protocol is set forth in the specification. One of ordinary skill in the art could reproduce the work without any problem. One need not use the same cell line as a source of the material, because as noted throughout the specification, this is a naturally-occurring, non-mutated gene. Hence, there are no issues as to reproducability. The specification clearly teaches how to obtain the material, and the examiner's remarks should be withdrawn.

The examiner has then rejected all of claims 183-191 under 35 USC §112, first paragraph, arguing that these claims do not satisfy the written description requirement. The rejection is traversed.

The examiner states, correctly, what the main claim recites, and also states, correctly, the relationship between tumor rejection antigen precursors and tumor rejection antigens.

The examiner also interprets examples 23 & 25 correctly, but fails to note that, in addition to MAGE 1, 2, 3, the MAGE 4, 5, 6, & 7 molecules are described in the specification, and all are encoded by nucleic acid molecules which hybridize to SEQ ID NO: 8. Hence, there are seven species within the specification which satisfy the requirement of the claims under the conditions of the claims. All of these molecules also satisfy the requirement that they be tumor rejection antigen precursors. Attached hereto is a copy of U.S. Patent No. 5,405,940, which demonstrates that all of the species are processed to form tumor rejection antigens. The USPTO has accepted the principle, and has issued a patent on the tumor rejection antigens. The scientific literature is replete with articles on the molecules, and their function as tumor rejection antigen precursors. A partial list is attached.

Hence, it cannot be denied that MAGE-1 through MAGE-7, inclusive, which are described in the specification, satisfy the claims.

Notwithstanding the disclosure of 7 species which satisfy the claim, the examiner cites to a non-prior art paper, arguing that this paper shows that the written description requirement is not satisfied.

First, appellate precedent precludes the examiner from relying on non-prior art in the context of a rejection under 35 USC §112, first paragraph. See In re Koller, 202 USPQ 702, 706 (CCPA. 1980), further citing In re Hogan, 194 USPQ 527 (CCPA 1977) ("Compliance with §112, paragraph 1, is to be judged as of the date the application is filed.") the paper relied upon on by the examiner supports applicants' position.

The examiner states that:

> "Ding, et al, Biochem. Biophys. Res. Commun. 202:549-555 (1994) disclose that homologous MAGE-1 can be polymorphic."

It is not contested that Ding states this; however, the examiner neglects to state the following, which appears three lines prior to the phrase he quotes:

> "A gene highly homologous to MAGE-1 was isolated which different from the published DNA sequence at positions 94 and 813. The position 94-A to G transition results in a threonine to alanine substitution while the position 813 mutation is silent."

Hence, the examiner is relying on a paper which shows one amino acid difference in the protein sequence, and two at the nucleotide sequence level.

A difference of two nucleotides over the stretch of the molecule will not impact the hybridization. The Ding MAGE-1 molecule would be expected to hybridize to SEQ ID NO: 8, because it differs from SEQ ID NO: 8 by less than the sequences disclosed in the specification. Further, the resulting protein, which differs by only one amino acid, does not impact the disclosed tumor rejection antigen at all. Hence, it is it not seen how the written description requirement can be deemed not to be satisfied.

The examiner cites to a series of cases, none of which are particularly relevant. For example, Vas-Cath, Inc. v. Mahurkar is cited for the principal that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date, he or she was in possession of the invention." At the time the application was filed, applicants had (i) disclosed what a tumor rejection antigen precursor was, (ii) described what a tumor rejection antigen was, (iii) had described relevant hybridization conditions and (iv) had reduced seven species to practice. If this is not possession if the invention, it is difficult to see what is.

The examiner then goes on to cite Fiers v. Revel and Amgen Inc. v. Chugai Pharmaceutical for the proposition that "conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required." With all due respect, since seven species of nucleic acid molecules have been described, the requirement is met, and these cases are not relevant. Nor are the remaining cases cited by the examiner relevant. In each case, there was no DNA described, and the claims were drawn, specifically to nucleic acid molecules.

The examiner's conclusions, at the bottom of page 4, simply ignore the facts. As noted, seven species are described in the specification. With respect to "polymorphism," all the examiner has

provided is a non-prior art reference which describes a molecule with one amino acid different from the MAGE-1 molecule described in the application. As has been pointed out, supra, the single change doesn't impact the tumor rejection antigen of MAGE-1. So, apart from the fact that the reference cannot be used, as a matter of law, the reference does not show lack of written description. The examiner's position cannot be maintained, and should be withdrawn.

The examiner then directs applicants to the "Guidelines for the Examination of Patent Applications Under the 35 USC §112 ¶1 Written Description Requirement." Applicants have studied these carefully. It is suggested that the examiner review Example 9 of these guidelines, and explain why it does not control, and why the claims should not per se be deemed to satisfy the written description in view of example 9.

Any failure to do so will result in a petition to the Group Director

Withdrawal of the rejection is proper, and is urged.

The examiner has also set forth a lack of enablement rejection, citing to Colbert v. Lofdahl for the proposition that "an alleged conception having no mail specificity than that is simply a wish to know the identity of any material with biological property." As has been pointed out, applicants reduced seven species to practice which possess the properties of what is claimed. They have no need to "wish to know" the identity of relevant materials. They do know the identity of relevant materials, and have set them forth. The examiner continues to rely on Ding, but as has been pointed out, supra, Ding does show a tumor rejection antigen precursor which satisfies the claims - even if it is non-prior art.

All of the remaining references cited by the examiner must be excluded as not constituting prior art, as the Federal Courts have pointed out. Even if they did constitute prior art, however, they do not change the fact that seven species within the claims are taught, and the reference relied upon by the examiner supports the claims as well.

As such, the rejection should be withdrawn.

Applicants need not and will not comment on points 8 & 9 of the action.

Withdrawal of the lack of enablement rejection, and allowance of the application are believed proper and are urged.

Respectfully submitted,

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